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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/600,854	06/20/2003	William Fenical	UCSD1530-2	8484

28213 7590 08/19/2005

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EXAMINER	
POWERS, FIONA	

ART UNIT	PAPER NUMBER
1626	

DATE MAILED: 08/19/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/600,854	FENICAL ET AL.	
	Examiner	Art Unit	
	Fiona T. Powers	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 June 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-6,15-21 and 27-44* is/are pending in the application.

4a) Of the above claim(s) *15-21 and 27-29* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-6 and 30-44* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

BD

Receipt is acknowledged of the amendment filed June 2, 2005, which has been entered in the file.

The disclosure is objected to because of the following informalities: applicants are asked to supply the missing ATCC Accession Number in paragraph [0012] on page 4 and paragraph [0040] on page 10.

Appropriate correction is required.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 2 to 6, 20 to 32 and 34 to 44 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Variables R_1, R_2 and R_3 are monovalent radicals but are defined as sulfonyl which is a divalent radical. It is not clear what else is bonded to the sulfonyl radical.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 2 to 6 and 30 to 44 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph are as follows:

1. the nature of the invention,
2. the state of the prior art,
3. the predictability or lack thereof in the art,
4. the amount of direction or guidance present,
5. the presence or absence of working examples,
6. the breadth of the claims,
7. the quantity of experimentation needed, and
8. the level of skill in the art.

See In re Wands, 8 USPQ2d 1400.

The nature of the invention is a pharmaceutical composition useful for inhibiting the proliferation of hyperproliferative mammalian cells and an article of manufacture which includes a label which indicates that the pharmaceutical composition can be used for treatment of cell proliferative disorders.

The state of the prior art is that the pharmacological art involves screening in vitro and in vivo to determine which compounds exhibit the desired pharmacological activities (i.e. what compounds can treat which specific diseases and by what mechanism). There is no absolute predictability even in view of the seemingly high level of skill in the art. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face.

It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. In re Fisher, 166 USPQ 18 indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute.

Applicants are claiming a pharmaceutical composition useful for inhibiting the proliferation of hyperproliferative mammalian cells and an article of manufacture which includes a label which indicates that the pharmaceutical composition can be used for treatment of cell proliferative disorders. This includes pharmaceutical composition useful for inhibiting cancer and articles with a label which indicates that it can be used to treat cancer. The state of the prior art is that cancer therapy remains highly unpredictable. The various types of cancers have

different causative agents, involve different cellular mechanisms, and consequently, differ in treatment protocol. It is known that the challenge of cancer treatment has been to target specific therapies to pathogenetically distinct tumor types, that cancer classification has been based on primarily on morphological appearance of the tumor and that tumors with similar histopathological appearance can follow significantly different clinical courses and show different responses to therapy (Golub et al. page 531). Furthermore, it is known that chemotherapy is most effective against tumors with rapidly dividing cells and that cells of solid tumors divide relatively slowly and chemotherapy is often less effective against them.

The only direction or guidance present in the instant specification is data on page 31 for inhibition of colon cancer cells.

The breadth of the claims is a pharmaceutical composition useful for inhibiting the proliferation of any hyperproliferative mammalian cells and an article of manufacture which includes a label which indicates that the pharmaceutical composition can be used for treatment of any cell proliferative disorder.

The quantity of experimentation needed is undue experimentation. One of skill in the art would need to

determine what hyperproliferative diseases would be benefited (treated) by and would then have to determine which of the claimed compounds would provide treatment of which hyperproliferative disease, if any.

The level of skill in the art is high. However, due to the unpredictability in the pharmaceutical art, it is noted that each embodiment of the invention is required to be individually assessed for physiological activity by in vitro and in vivo screening to determine which compounds exhibit the desired pharmacological activity and which diseases would benefit from this activity.

Thus, the specification fails to provide sufficient support of the broad use of the compound of the instant claims in a pharmaceutical composition useful for inhibiting proliferation of hyperproliferative mammalian cells. As a result necessitating one of skill to perform an exhaustive search for which hyperproliferative diseases can be treated by what pharmaceutical composition of the instant claims in order to practice the claimed invention.

Genetech Inc. v. Novo Nordisk A/S 42 USPQ2d 1001 states that "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "patent protection is granted in return for an enabling

disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Therefore, in view of the Wands factors and In re Fisher discussed above, to practice the claimed invention herein, one of skill in the art would have to engage in undue experimentation to test which diseases can be treated by the compound encompassed in the instant claims, with no assurance of success.

This rejection can be overcome if the claims were limited to a pharmaceutical composition useful for inhibiting the proliferation of colon cancer cells and the article of manufacture comprises a label which indicates that the pharmaceutical composition can be used for the treatment of colon cancer.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 31 to 44 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fenical et al. (WO 02/047610).

Determination of the scope and content of the prior art (MPEP §2141.01)

The reference discloses the compound of the formula I wherein E_1, E_3 and E_4 are O, E_2 is NH, R_1 is chloroethyl, R_2 is methyl, R_3 is hydroxy and x is 0. Note Figure 1. The reference also discloses that the compound (known as salinosporamide A) has pharmaceutical activity as a potent anticancer agent. Note page 9, last paragraph to page 10, first paragraph.

Ascertainment of the difference between the prior art and the claims (MPEP §2141.02)

The difference between the reference and what is claimed is that the reference does not disclose a pharmaceutical composition containing the compound.

Finding of prima facie obviousness---rational and motivation (MPEP §2142-2413)

However, since the compound has pharmaceutical activity it would have been obvious to one of ordinary skill in the art to prepare a pharmaceutical composition containing the compound. One of ordinary skill in the art would have been motivated to make the claimed composition with the expectation that pharmaceutical compositions with anticancer activity would be obtained.

Applicant's arguments filed June 2, 2005 have been fully considered but they are not persuasive.

Applicants argue that substituents R_1-R_3 may be polyvalent and that those skilled in the art would clearly understand that

the bond of the sulfonyl radical which is not connected to the main structure of compound I can be substituted as is reasonable and chemically feasible. However, in the compound I substituents R_1-R_3 have one attachment to the main structure thus they are clearly monovalent. It is not for one of skill in the art to determine what could be attached to the other bond of the sulfonyl radical this should be clearly set forth in the specification.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Fiona T. Powers whose telephone number is 571-272-0702. The examiner can normally be reached on Monday - Friday 8:00 AM to 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph K. McKane can be reached on 571-272-0699. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Fiona T. Powers
Primary Examiner
Art Unit 1626

ftp
August 15, 2005